IN THE SPECIFICATION:

Replace [0001] as follows:

CLAIM TO DOMESTIC PRIORITY

[0001] This Application is a U.S. National Stage Application filed under 35 U.S.C. 371 claiming priority from the International Application No. PCT/US03/07073, filed March 6, 2003, which claims the benefit of United States Provisional Patent Application Serial No. 60/362,247, filed March 6, 2002, and which applications are incorporated herein by reference. ~~The present non-provisional patent application claims priority to provisional application serial no. 60/362,247, entitled "A Novel Oral Adjuvant: Immunostimulatory Effect of HIV-Derived P1 Peptide," filed on March 6, 2002, by Nobuyuki Matoba, Charles J. Arntzen and Tsafrir Mor.~~

Replace [0006] as follows:

[0006] Subunit vaccines, especially those vaccines that target the mucosal ~~muscosal~~ immune system, are viable, safe and effective alternatives. Mucosal vaccines ~~require~~ do not require injection; thus, risk of transmission of infection is minimal. Finally, mucosal vaccines elicit immune response both systemically and mucosally.

Replace [0027] as follows:

[0027] FIG. 1 depicts the structure of an HIV retrovirus. HIV retrovirus 10 is an enveloped retrovirus. HIV retrovirus 10 is comprised of a viral membrane 12, ampiphilic regions 14, charged helices 16, calcium (Ca^{2+}) binding sites 18, gp41 subunits 20, and gp120 subunits 22. Adjuvant peptide 24 facilitates HIV transcytosis across mucosal barriers toward the serosal environment by binding to galactosyl ceramide (GalCer) on the surface of mucosal ~~muscosal~~ epithelial cells.

Replace [0028] as follows:

[0028] Adjuvant peptide 24 comprises 36 amino acids (SEQ. ID. NO: 1) corresponds ~~correspondes~~ to a portion of the gp41 envelope. This peptide includes a conserved epitope (SEQ. ID. NO: 2), which is recognized by the neutralizing human IgG 2F5 and secretory IgAs that functionally neutralize HIV transcytosis through epithelial cells. The conserved aromatic residues are important for GalCer binding.

Replace [0029] as follows:

[0029] FIG. 2 depicts the structure of an adjuvant 30 according to one embodiment. Adjuvant 30 comprises peptides 32, linkers 34, and cargo proteins 36. However,[an] alternate embodiments ~~envisions~~ envision adjuvant 30 comprising at least peptides 32, but not necessarily linkers 34 and cargo proteins 36. Peptides 32 may comprise adjuvant peptides as one or more portions of P1 peptides, P5 peptides, or their functional equivalents. In one embodiment, cargo protein 36 is an antigen, for example cholera toxin. In an alternate embodiment, cargo protein 36 is any protein to be delivered to an animal cell.

Replace [0030] as follows:

[0030] According to one embodiment, an adjuvant peptide is a portion of the P1 peptide, HIV envelope protein gp41, which includes the conserved epitope, lectin binding site (SEQ. ID. NO: 2). According to an alternate embodiment, the ~~adjuvnat~~ adjuvant peptide is a portion of the P5 peptide, HIV envelope protein gp41 which includes the P1 peptide and a calcium binding site (residue number 622-684). P1 and P5 peptides also include their functional equivalents.

Replace [0031] as follows:

[0031] Functional equivalents of adjuvant peptides include peptides or portions of larger proteins with overall sequence or structural similarity to P1 or P5 peptides, and their derivatives,

which allow the functionality disclosed here, including, but not limited to, one or more of the following: ~~the enhancing~~ enhancing the immune response, GalCer binding, binding to the surface of cells containing GalCer, endocytosis to such cells or transcytosis across a tight cell barrier.

Replace [0035] as follows:

[0035] Example 1 demonstrates that ~~adjvuant~~ adjuvant peptide enhances immune responses against cholera toxin B subunit by mucosal co-administration of adjuvant peptide and cholera toxin B subunit. Synthetic adjuvant peptide (SEQ. ID. NO: 3) with a C-terminal $CONH_2$, was synthesized by Eurogentec (Belgium) and by the Protein Chemistry Laboratory at Arizona State University. A ~~cystine~~ cysteine residue was added to the beginning of SEQ. ID. NO: 1 to allow for dimerization (residue 649). Cholera Toxin B (CTB) subunit was chosen for co-administration because it is non-toxic and it is a strong mucosal adjuvant. Additionally, CTB binds to G_{M1} ganglioside whereby being able to target the fused antigen to mucosa.

Replace [0038] as follows:

[0038] Samples were serially diluted in phosphate buffered saline containing 0.05% Tween-20 (PBST) containing 1% nonfat dry milk. Plates were coated with CTB overnight at 4°C, blocked with PBST containing 5% nonfat dry milk and then incubated with samples. Antibodies were detected by horseradish peroxidase-conjugated secondary antiisotypic antisera against the appropriate mouse antibodies (rabbit anti-mouse total IgG from CalBiochem, and the following anti mouse antisera: Anti-IgG_1, anti-IgG_{2a}, anti-IgG_{2b}, anti-IgG_3 from Santa Cruz Biotechnology; and anti-IgA from Sigma. FIG. 3A-3C ~~shown~~ show maximal dilutions that allowed quantification.

Replace [0039] as follows:

[0039] FIG. 4 illustrates the end point of anti-CTB antibodies four weeks after immunization. Chemiluminescent ELISA was conducted as described in FIG. 3. Titers in FIG. 4 are defined as reciprocals of the highest dilution giving a positive A_{490} reading above 0.1. FIG.

5 illustrates, for example, reciprocal dilution of serum IgG_1. FIG. 6 illustrates subclass titers of total IgG, IgG_1, IgG_{2a}, IgG_{2b}, IgG_3 and IgA.

Replace [0040] as follows:

[0040] While in FIG. 4 antibody titers were below detection levels, co-administration of P1 and CTB to mice resulted in significantly higher titers of anti-CTB antibodies as compared to mice that were given CTB alone. Specifically, in FIG. 3, the level of fecal and vaginal anti-CTB IgA in the second and third week and serum ~~andti-CTB~~ anti-CTB in the second, third and fourth week appeared to be higher in mice fed P1 with CTB than in mice fed only CTB. Moreover, as illustrated in FIG. 6, co-administration of P1 with CTB resulted in increasing all serum anti-CTB IgG subclass (IgG_1, IgG_{2a}, IgG_{2b}, IgG_3) titers by five to ten times in the fourth week, as compared to administration of CTB alone, as shown in FIG. 4.

Replace [0041] as follows:

[0041] Therefore, P1 peptide was shown to augment the production of mucosal IgA and serum IgG to co-administered CTB. Because CTB is a strong mucosal immunogen by itself, the increase of both anti-CTB IgG_1 and IgG_{2a} levels suggest that the immune enhancement effect of P1 peptide is attributable to activating both Th1 and Th2 response. Th1 and Th2 response is illustrated in FIG. 7. IgG2a 40 effects T1 response 38 through cell-mediated immunity, targeting intracellular pathogens 42. Antibodies 46, such as IgG_1 and IgA, effect ~~affect~~ Th2 response 44 targeting extracellular parasites, viruses and bacteria 48. Secondly, P1 peptide did not induce antibody production against itself, even in the presence of CTB. Therefore, P1 peptide can be used a mucosal adjuvant to enhance immune response in living organisms.

Replace [0044] as follows:

[0044] FIG. 9 depicts maps of plasmids comprised of DNA sequences of CTB, P1, CTB-P1 fusion and for the plant-expression of the CTB-P1 fusion protein. A plant-expression optimized DNA molecule encoding for P1 peptide was synthesized. The sequence was inserted behind a portion of the gene encoding the C-terminus of the CTB molecule behind a DNA spacer

encoding a Glycine-Proline-Glycine-Proline (GPGP) hinge. An endoplasmic reticulum (ER) retention signal was engineered at the Carboxyl-Terminus. The PCR product was ~~closed~~ cloned into the cloning vector TOPO2.1 (Invitrogen) to create pTM058.